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Socioeconomic and demographic inequalities in stage at diagnosis and survival among colorectal cancer patients: evidence from a Swiss population-based study

Feller, Anita ; Schmidlin, Kurt ; Bordoni, Andrea ; Bouchardy, Christine ; Bulliard, Jean-Luc ; Camey, Bertrand ; Konzelmann, Isabelle ; Maspoli, Manuela ; Wanner, Miriam ; Zwahlen, Marcel ; Clough-Gorr, Kerri M

Abstract: Socioeconomic inequalities in cancer stage at diagnosis and survival are important public health issues. This study investigates the association between socioeconomic position (SEP) and colorectal cancer (CRC) stage at diagnosis and survival in Switzerland, a European country with highest level of medical facilities and life expectancy. We used population-based CRC data from seven Swiss cantonal cancer registries 2001-2008 (N = 10,088) linked to the Swiss National Cohort (SNC). Follow-up information was available until the end of 2013. SEP was estimated based on education. The association between cancer stage and SEP was assessed using logistic regression models including cancer localization (colon/rectum), sex, age, civil status, urbanity of residence, language region, and nationality (Swiss/non-Swiss). Survival was analyzed using competing risk regressions reporting subhazard ratios (SHRs) for the risk of dying due to CRC. We observed a social gradient for later stage CRC with adjusted odds ratios (ORs) of 1.11 (95% CI: 0.97-1.19) and 1.28 (95% CI: 1.08-1.50) for middle and low SEP compared to high SEP. Further, single compared to married people had elevated odds of being diagnosed at later stages. Survival was lower in patients with CRC with low SEP in the unadjusted model (SHR: 1.18, 95% CI: 1.07-1.30). After adjustment for stage at diagnosis and further sociodemographic characteristics, significant survival inequalities by SEP disappeared but remained for non-Swiss compared to Swiss citizens and for patients living in nonurban areas compared to their urban counterparts. Swiss public health strategies should facilitate equal access to CRC screening and optimal CRC care for all social groups and in all regions of Switzerland.

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APPENDIX

Suppl. Table 1: Distribution of socioeconomic and demographic characteristics of the cantons participating in the study and all Switzerland (population aged 30-84 years), Census 2000

Socioeconomic and demographic characteristics	Cantons participating in the study		Whole of Switzerland	
	N	column %	N	column %
Socioeconomic position (SEP)				
low SEP	489,870	23.8	1,078,424	23.7
middle SEP	999,265	48.5	2,331,895	51.3
high SEP	507,472	24.6	1,010,800	22.2
unknown	64,338	3.1	124,213	2.7
Sex				
male	991,467	48.1	2,202,279	48.5
female	1,069,478	51.9	2,343,053	51.6
Age at diagnosis				
30-49 years	1,039,029	50.4	2,287,496	50.3
50-64 years	590,850	28.7	1,288,317	28.3
65-74 years	284,981	13.8	637,993	14.0
75-84 years	146,085	7.1	331,526	7.3
Civil status				
single	321,193	15.6	683,058	15.0
married	1,393,206	67.6	3,134,345	69.0
widowed	143,630	7.0	323,982	7.1
divorced	202,916	9.9	403,947	8.9
Urbanity of residence				
urban	712,110	34.6	1,309,476	28.8
peri-urban	1,021,000	49.5	2,059,108	45.3
rural	327,835	15.9	1,176,748	25.9
Language-region				
German-speaking region	877,042	42.6	3,278,361	72.1
French-speaking region	980,809	47.6	1,054,883	23.2

Italian-speaking region	203,094	9.9	212,088	4.7
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Nationality

Swiss	1,585,929	77.0	3,700,941	81.4
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non-Swiss	475,016	23.1	844,391	18.6
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Total	N	row %	2,060,945	45.3	4,545,332	100.0
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Suppl. Table 2: Contribution of colorectal cancer cases and person-years by cancer registry: incidence period 05/12/2000 - 31/12/2008, patients aged 30-84 years at diagnosis

CR	all stages			with stage information		
	Cases (N)	Person-years (PY) of follow-up	% of pooled PY	Cases (N)	Person-years (PY) of follow-up	% of pooled PY
Fribourg	294	1,344	2.4	277	1,273	2.4
Geneva	1,214	7,250	12.8	1,147	7,016	13.4
Neuchâtel	601	3,284	5.8	540	3,125	6.0
Ticino	1,276	7,216	12.7	1,224	6,967	13.3
Valais	910	5,043	8.9	855	4,771	9.1
Vaud	2,021	11,754	20.7	1,704	10,064	19.2
Zurich	3,772	20,766	36.7	3,400	19,298	36.7

Note: 82 cases (0.8%) out of originally 10,170 cases aged 30-84 years have been excluded due to missing SEP information. From the remaining dataset (N=10,088), 140 (1.4%) additional cases were excluded for survival analyses due to zero survival time (death certificate only cases or cases first diagnosed at autopsy).

1 **Suppl. Table 3:** Odds ratios (OR) of later colorectal cancer stage at diagnosis (Stage I-II versus Stage III-IV)

	Model 1		Model 2		Model 3		Model 4		Model 5*	
	OR	[95%CI]	OR	[95%CI]	OR	[95%CI]	OR	[95%CI]	OR	[95%CI]
SEP										
High SEP (ref.)										
Middle SEP	1.00	[0.90-1.12]	1.00	[0.90-1.11]	1.00	[0.90-1.12]	1.00	[0.90-1.12]	0.99	[0.90-1.11]
Low SEP	1.05	[0.94-1.19]	1.05	[0.93-1.19]	1.05	[0.92-1.19]	1.05	[0.92-1.19]	1.04	[0.92-1.19]
Sex										
male (ref.)										
female			1.12	[1.03-1.23]	1.12	[1.03-1.23]	1.12	[1.03-1.23]	1.12	[1.03-1.23]
Age at diagnosis										
50-64 years (ref.)										
< 50 years			1.36	[1.14-1.63]	1.37	[1.14-1.64]	1.36	[1.14-1.64]	1.37	[1.14-1.64]
65-74 years			0.95	[0.85-1.06]	0.95	[0.86-1.06]	0.95	[0.86-1.06]	0.95	[0.86-1.06]
75-84 years			0.89	[0.80-1.00]	0.89	[0.80-1.00]	0.89	[0.80-1.00]	0.89	[0.80-1.00]
Civil status										
married (ref.)										
single			1.32	[1.13-1.53]	1.31	[1.13-1.53]	1.31	[1.13-1.53]	1.31	[1.13-1.53]
widowed			0.94	[0.82-1.07]	0.94	[0.82-1.06]	0.94	[0.82-1.07]	0.94	[0.82-1.07]
divorced			1.09	[0.95-1.25]	1.08	[0.94-1.25]	1.08	[0.94-1.25]	1.09	[0.95-1.25]
Nationality										
Swiss (ref.)										
Non-Swiss			1.07	[0.96-1.20]	1.07	[0.96-1.20]	1.07	[0.96-1.20]	1.07	[0.96-1.21]
Urbanity										
urban (ref.)										
peri-urban					0.98	[0.89-1.07]	0.98	[0.89-1.07]	0.98	[0.89-1.07]
rural					1.01	[0.88-1.15]	1.00	[0.88-1.15]	1.00	[0.87-1.15]
Language region**										
German (ref.)										
French					1.03	[0.94-1.12]	1.03	[0.94-1.12]	0.99	[0.76-1.31]

Italian	0.97	[0.85-1.10]	0.97	[0.85-1.10]	0.98	[0.86-1.11]
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Localisation

Colon (ref.)

rectum	0.99	[0.90-1.08]	0.99	[0.90-1.08]
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* Additionally adjusted for canton of residence to account for unmeasured canton characteristics associated with SEP and stage.

**German-speaking region: eastern parts of the canton of Fribourg, eastern parts of the canton of Valais (upper Valais), canton of Zurich; French-speaking region: western parts of the canton of Fribourg, canton of Geneva, canton of Neuchâtel, western parts of the canton of Valais (Central and Lower Valais), canton of Vaud; Italian-speaking region: canton of Ticino.

1 **Suppl. Table 4:** Odds ratios (OR) of later colorectal cancer stage at diagnosis (Stage I-III versus Stage IV)

	Model 1		Model 2		Model 3		Model 4		Model 5*	
	OR	[95%CI]	OR	[95%CI]	OR	[95%CI]	OR	[95%CI]	OR	[95%CI]
SEP										
High SEP (ref.)										
Middle SEP	1.03	[0.91-1.18]	1.05	[0.92-1.20]	1.05	[0.92-1.20]	1.06	[0.92-1.21]	1.05	[0.92-1.20]
Low SEP	1.00	[0.86-1.15]	1.02	[0.88-1.19]	1.00	[0.86-1.17]	1.01	[0.87-1.18]	0.98	[0.84-1.15]
Sex										
male (ref.)										
female			1.02	[0.92-1.14]	1.03	[0.92-1.15]	1.01	[0.90-1.12]	1.02	[0.91-1.14]
Age at diagnosis										
50-64 years (ref.)										
< 50 years			1.20	[0.98-1.48]	1.21	[0.99-1.49]	1.21	[0.98-1.48]	1.21	[0.99-1.49]
65-74 years			0.93	[0.82-1.06]	0.94	[0.82-1.06]	0.92	[0.81-1.05]	0.93	[0.81-1.05]
75-84 years			0.92	[0.80-1.05]	0.92	[0.80-1.05]	0.89	[0.77-1.02]	0.90	[0.78-1.03]
Civil status										
married (ref.)										
single			1.25	[1.05-1.48]	1.24	[1.04-1.47]	1.24	[1.04-1.48]	1.25	[1.05-1.49]
widowed			0.90	[0.76-1.07]	0.89	[0.76-1.06]	0.90	[0.76-1.06]	0.90	[0.76-1.07]
divorced			1.21	[1.03-1.42]	1.20	[1.03-1.42]	1.21	[1.02-1.42]	1.23	[1.04-1.45]
Nationality										
Swiss (ref.)										
Non-Swiss			1.09	[0.95-1.24]	1.07	[0.94-1.23]	1.07	[0.93-1.23]	1.09	[0.95-1.25]
Urbanity										
urban (ref.)										
peri-urban					0.95	[0.85-1.07]	0.95	[0.85-1.07]	0.96	[0.86-1.08]
rural					0.99	[0.85-1.16]	0.98	[0.83-1.15]	0.92	[0.78-1.09]
Language region**										
German (ref.)										
French					1.15	[1.03-1.28]	1.14	[1.02-1.28]	1.03	[0.76-1.41]

Italian	1.18	[1.01-1.38]	1.16	[0.99-1.36]	1.21	[1.03-1.42]
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Localisation

Colon (ref.)

rectum	0.74	[0.66-0.82]	0.74	[0.66-0.83]
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1	* Additionally adjusted for canton of residence to account for unmeasured canton characteristics associated with SEP and stage.
2	**German-speaking region: eastern parts of the canton of Fribourg, eastern parts of the canton of Valais (upper Valais), canton of Zurich; French-
3	speaking region: western parts of the canton of Fribourg, canton of Geneva, canton of Neuchâtel, western parts of the canton of Valais (Central
4	and Lower Valais), canton of Vaud; Italian-speaking region: canton of Ticino.
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2 **Suppl. Table 5.** Cause-specific hazard ratios (CHR) in patients with colorectal cancer

	colorectal cancer death		death due to other causes	
	CHR	[95%CI]	CHR	[95%CI]
SEP				
High SEP (ref.)				
Middle SEP	1.01	[0.92-1.12]	1.16	[1.00-1.34]
Low SEP	1.12	[1.00-1.25]	1.24	[1.02-1.71]
Sex				
male (ref.)				
female	0.93	[.0.86-1.01]	0.65	[0.58-0.73]
Age at diagnosis				
50-64 years (ref.)				
< 50 years	0.68	[0.57-0.81]	0.47	[30.38-72.03]
65-74 years	1.25	[1.13-1.37]	2.29	[1.94-1.21]
75-84 years	2.00	[1.81-2.20]	15.48	[1.35-1.62]
Civil status				
married (ref.)				
single	1.04	[0.92-1.19]	1.14	[1.00-1.29]
widowed	0.99	[0.88-1.11]	0.89	[0.79-1.00]
divorced	1.00	[0.88-1.13]	1.10	[0.98-1.24]
Nationality				
Swiss (ref.)				
Non-Swiss	1.23	[1.10-1.36]	1.15	[1.04-1.27]
Urbanity				
urban (ref.)				
peri-urban	1.16	[1.07-1.26]	1.04	[0.93-1.16]
rural	1.15	[1.02-1.30]	1.01	[0.85-1.19]

Language region*

German (ref.)

French	0.96	[0.77-1.20]	1.00	[0.70-1.43]
Italian	0.93	[0.82-1.04]	1.02	[0.88-1.19]

Localisation

Colon (ref.)

rectum	1.11	[1.02-1.19]	1.01	[0.91-1.13]
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Stage at diagnosis

Stage I (ref.)

Stage II	3.24	[2.57-4.08]	1.08	[0.95-1.24]
Stage III	8.34	[6.70-10.39]	1.03	[0.89-1.19]
Stage IV	35.50	[28.54-44.16]	2.12	[1.77-2.53]

¹*German-speaking region: eastern parts of the canton of Fribourg, eastern parts of the canton of Valais (upper Valais), canton of Zurich; French-speaking region: western parts of the canton of Fribourg, canton of Geneva, canton of Neuchâtel, western parts of the canton of Valais (Central and Lower Valais), canton of Vaud; Italian-speaking region: canton of Ticino.

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1 **Suppl. Table 6:** Odds ratios (OR) of later colorectal cancer stage at diagnosis after multiple imputation of
2 stage

	Stage I versus Stage II-IV		Stage I-II versus Stage II-IV		Stage I-III versus Stage IV	
	OR	[95%CI]	OR	[95%CI]	OR	[95%CI]
SEP						
High SEP (ref.)						
Middle SEP	1.11	[0.97-1.28]	1.01	[0.90-1.12]	1.06	[0.92-1.21]
Low SEP	1.29	[1.10-1.52]	1.06	[0.93-1.20]	1.00	[0.85-1.16]
Sex						
male (ref.)						
Female	1.05	[0.93-1.18]	1.12	[1.02-1.22]	1.01	[0.91-1.13]
Age at diagnosis						
50-64 years (ref.)						
< 50 years	1.16	[0.92-1.48]	1.32	[1.11-1.58]	1.18	[0.97-1.44]
65-74 years	1.02	[0.89-1.17]	0.95	[0.86-1.06]	0.94	[0.83-1.07]
75-84 years	1.18	[1.02-1.37]	0.93	[0.83-1.04]	0.97	[0.84-1.11]
Civil status						
married (ref.)						
Single	1.37	[1.11-1.68]	1.34	[1.15-1.55]	1.31	[1.10-1.55]
Widowed	1.05	[0.87-1.25]	0.94	[0.82-1.07]	0.89	[0.75-1.06]
Divorced	1.17	[0.97-1.41]	1.11	[0.97-1.27]	1.26	[1.07-1.48]
Nationality						
Swiss (ref.)						
Non-Swiss	1.02	[0.88-1.19]	1.07	[0.95-1.20]	1.08	[0.94-1.23]
Urbanity						
urban (ref.)						
peri-urban	0.93	[0.82-1.04]	0.97	[0.89-1.07]	0.96	[0.86-1.07]
Rural	0.96	[0.80-1.15]	1.00	[0.87-1.14]	0.93	[0.79-1.09]

Language region

German (ref.)

French	1.16	[0.82-1.66]	0.99	[0.75-1.30]	1.03	[0.76-1.40]
Italian	0.92	[0.78-1.09]	0.96	[0.84-1.10]	1.16	[0.99-1.36]

Localisation

Colon (ref.)

Rectum	0.68	[0.61-0.76]	0.99	[0.91-1.08]	0.74	[0.67-0.83]
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UICC stage was imputed with 25 imputations using the following variables as predictors: age at diagnosis and follow-up time as continuous predictors, SEP, sex, civil status, nationality, urbanity, language region, tumour localisation and follow-up status (alive, death due to CRC, other cause of death) as categorical predictors³², and an interaction term between follow-up time and follow-up status³³. All models have been additionally adjusted for canton of residence.

¹ German-speaking region: eastern parts of the canton of Fribourg, eastern parts of the canton of Valais (upper Valais), canton of Zurich; French-speaking region: western parts of the canton of Fribourg, canton of Geneva, canton of Neuchâtel, western parts of the canton of Valais (Central and Lower Valais), canton of Vaud; Italian-speaking region: canton of Ticino.

1 **Suppl. Table 7:** Sub-hazard ratios and 95% confidence intervals (95%CI), risk of colorectal cancer death in
2 colorectal cancer patients after multiple imputation of stage

Final Model		
	SHR	[95%CI]
SEP		
High SEP (ref.)		
Middle SEP	1.00	[0.91-1.11]
Low SEP	1.10	[0.99-1.24]
Sex		
male (ref.)		
female	0.96	[0.88-1.04]
Age at diagnosis		
50-64 years (ref.)		
< 50 years	0.69	[0.58-0.81]
65-74 years	1.19	[1.08-1.30]
75-84 years	1.70	[1.54-1.87]
Civil status		
married (ref.)		
single	1.01	[0.88-1.15]
widowed	0.96	[0.85-1.08]
divorced	1.03	[0.91-1.16]
Nationality		
Swiss (ref.)	1.20	[1.09-1.34]
Non-Swiss		
Urbanity		
urban (ref.)		
peri-urban	1.13	[1.04-1.23]
rural	1.18	[1.05-1.32]

Language region*

German (ref.)

French 0.96 [0.77-1.20]

Italian 0.90 [0.80-1.02]

Localisation

Colon (ref.)

rectum 1.11 [1.03-1.20]

Stage at diagnosis

Stage I (ref.)

Stage II 2.88 [2.31-3.60]

Stage III 7.05 [5.69-8.73]

Stage IV 24.93 [20.17-30.80]

UICC stage was imputed with 25 imputations using the following variables as predictors: age at diagnosis and follow-up time as continuous predictors, SEP, sex, civil status, nationality, urbanity, language region, tumour localisation and d follow-up status (alive, death due to CRC, other cause of death) as categorical predictors³², and an interaction term between follow-up time and follow-up status³³.

Survival was analysed using competing risk regressions based on Fine and Gray's proportional hazard model³⁰. All underlying causes of death other than colorectal cancer (CRC) were classified as competing risks. The model has been adjusted for all variables listed plus canton of residence. Results are reported as sub-hazard ratios for risk of dying due to CRC (SHRs) with 95% confidence intervals (95%CI).

*German-speaking region: eastern parts of the canton of Fribourg, eastern parts of the canton of Valais (upper Valais), canton of Zurich; French-speaking region: western parts of the canton of Fribourg, canton of Geneva, canton of Neuchâtel, western parts of the canton of Valais (Central and Lower Valais), canton of Vaud; Italian-speaking region: canton of Ticino.